

Malignant transformation of multiple adnexal tumors in a Filipino-American patient with Brooke-Spiegler Syndrome: a case report

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ABSTRACT

INTRODUCTION Trichoepithelioma is a benign hamartoma which may exhibit similar clinical and histopathological features with basal cell carcinoma. Since prognosis is dissimilar, differentiating between them is important. Literature reveals fifteen reports of malignant transformation of multiple trichoepitheliomas into basal cell carcinoma, with none in the local setting. In Brooke-Spiegler syndrome, the incidence rate of malignant transformation of benign neoplasms has been reported in 5–10 % of patients.

CASE REPORT A 53-year-old Filipino-American female presented with multiple discrete to coalesced, well-defined, skin-colored to hyperpigmented, smooth, dome-shaped, rubbery papules and nodules on the face since childhood. Throughout the years, lesions increased in number and size and spread to the scalp, chest, abdomen, back, upper and posterior right thigh. Some developed ulceration, telangiectasia and pigmentation.

Chest radiography, radiographs of the jaw, whole abdominal ultrasound, cranial CT scan, ophthalmology and otorhinolaryngology assessments were normal. Based on clinical and histopathologic findings, the final diagnosis was Brooke-Spiegler syndrome with transformation into basal cell carcinoma. Carbon dioxide (CO₂) laser was used to excise large and ulcerated lesions with good cosmetic results.

CONCLUSION A case of a Filipino-American adult female diagnosed clinically and histologically with Brooke-Spiegler syndrome with transformation into basal cell carcinoma was presented. Given the similarities in clinical and histopathologic features of trichoepithelioma and basal cell carcinoma, accurate diagnosis should be made because of their difference in prognosis. The use of an acceptable treatment modality such as carbon dioxide (CO₂) laser in this case is an important emerging field of study.

KEYWORDS trichoepithelioma, basal cell carcinoma, Brooke-Spiegler syndrome, malignant transformation, carbon dioxide laser

INTRODUCTION

Trichoepitheliomas present as benign symmetrical, skin-colored papules, nodules or tumors commonly on the face, specifically the nasal area and nasolabial folds.¹ Malignant transformation rarely occurs, but there have been reports of basal cell carcinomas arising adjacent to trichoepitheliomas.² Treatment has been debated due to varied results.

This case describes a 53-year-old Filipino American female who has presented with multiple discrete to coalesced, well-defined, skin-colored, smooth, dome-shaped, rubbery papules on the face since childhood. Interval history revealed spread of lesions to the scalp, neck, back, chest, abdomen, and extremities. Some of the lesions evolved into nodules and tumors, which developed pigmentation, telangiectasia, and ulceration. Biopsies showed trichoepithelioma and

basal cell carcinoma.

CASE REPORT

A 53-year-old Filipino-American female presented with multiple asymptomatic papules, nodules, and tumors over the face, scalp, neck, back, chest, abdomen, upper extremities, and posterior right thigh. Lesions developed at eight years of age, initially presenting as few asymptomatic skin-colored papules on the nasal grooves measuring approximately 0.2x0.2 cm. There was gradual increase in size and number of papules, some evolving into nodules, which spread to the other areas of the face, scalp, neck, back, chest, abdomen, upper extremities, and posterior right thigh. No consultations were done. One year prior to consultation, some of the facial papules evolved into nodules and tumors. Some of the lesions developed telangiectasia, pigmentation,

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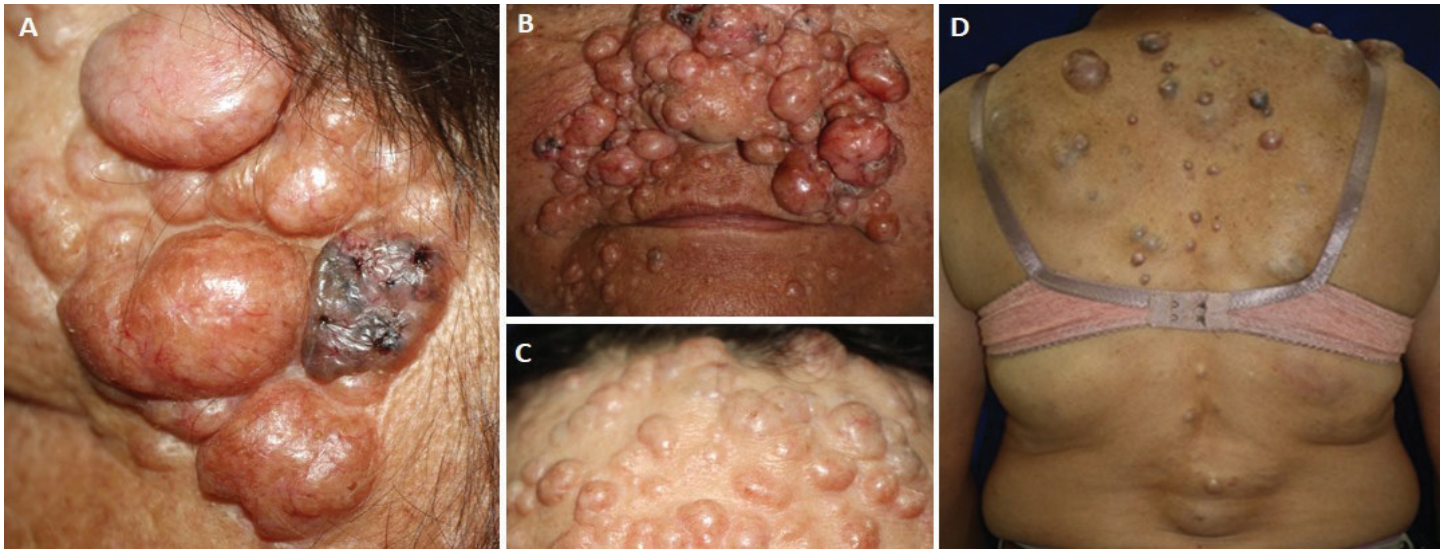


Figure 1. A-C. Multiple discrete to coalesced, well-defined, skin-colored to hyperpigmented, smooth-surfaced, dome-shaped, rubbery papules, nodules, and tumors, some with telangiectasia and ulceration on the face and D. back.

and ulceration; hence, prompting consultation.

Past medical history was unremarkable. She had a nine pack-years smoking history. None of her known family members had similar-looking lesions. She has been working as a street sweeper for thirteen years and previously as a tricycle driver for eighteen years. In both occupations, she worked outdoors for prolonged periods without sun protection.

Physical examination revealed multiple discrete to coalesced, well-defined, skin-colored to hyperpigmented, smooth, dome-shaped, rubbery papules, nodules, and tumors, some with telangiectasia and ulceration on the face (Figure 1A-C), scalp, neck, back (Figure 1D), chest, abdomen, upper extremities, and posterior right thigh. The smallest lesion was on the face (0.5 x 0.8 cm) whereas the largest was on the back (10 x 12 cm).

Dermoscopy of a skin-colored nodule on the forehead (Figure 2A) revealed thin, arborizing vessels amidst an ill-defined shiny white background (Figure 2B), features suggestive of trichoepithelioma. Dermoscopy of a skin-colored nodule with hyperpigmented areas and telangiectasia on the right cheek (Figure 2C) revealed ill-defined blue-gray ovoid nests and telangiectasia (Figure 2D), features consistent with basal cell carcinoma.

Histologic examination of a small skin-colored papule revealed tumor islands of basaloid cells with a lacelike pattern, embedded in a fibrous stroma in the dermis (Figure 3A-B). Microsections of three pigmented ulcerated nodules and tumors showed asymmetrical tumors islands of atypical basaloid cells surrounded by retraction artifacts with focal areas of necrosis, melanin, and melanophages, that are embedded in a fibromyxoid stroma (Figure 3D-E). Findings from the former revealed

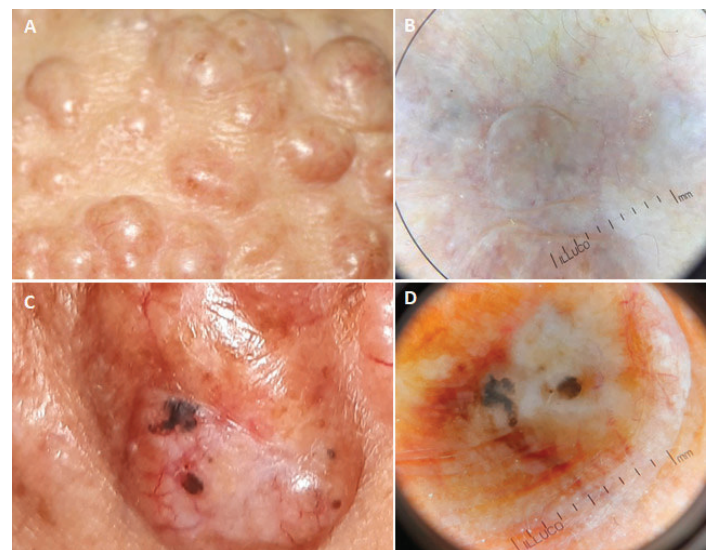


Figure 2. Dermoscopy of a A. skin-colored nodule on forehead shows B. small, thin, in-focus arborizing vessels amidst an ill-defined shiny white background, while a C. skin-colored nodule with hyperpigmented areas and telangiectasia on the right cheek shows D. ill-defined blue-gray ovoid nests, flecks of pigment, and telangiectasia.

trichoepithelioma, while the latter revealed basal cell carcinoma. BerEP4 staining was negative (Figure 3C) for the trichoepithelioma and positive (Figure 3F) for the basal cell carcinoma.

Chest radiography, panoramic radiograph of the jaw, whole abdominal ultrasound, and cranial CT scan were normal. To exclude obstruction on other organs, she was referred for ophthalmologic and otorhinolaryngologic examinations, which

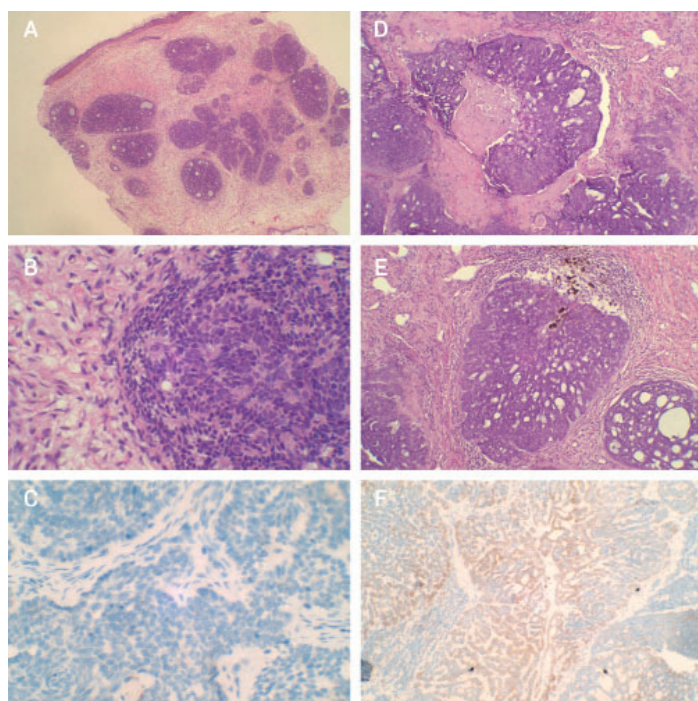


Figure 3. Histology of a skin-colored papule reveals **A.** tumor islands of basaloid cells throughout the dermis (H&E stain; 4x) **B.** lacelike network of basaloid cells embedded in a fibrous stroma (H&E stain; 40x), and **C.** negative BerEP4 staining (40x); Histology of hyperpigmented ulcerated nodules and tumors with telangiectasia reveal **D.** An asymmetrical tumor containing islands of basaloid cells, with focal areas of necrosis surrounded by retraction artifacts (H&E stain; 10x), **E.** melanin and melanophages within and around the basaloid cells embedded in a fibromyxoid stroma (H&E stain; 10x), and **F.** positive BerEP4 staining (40x).

revealed normal findings. A final diagnosis of Brooke-Spiegler syndrome with transformation into basal cell carcinoma was given. The pigmented and ulcerated lesions were removed and debulked using ablative CO₂ laser with good healing and cosmetic result (Figure 4A-D). She has undergone a total of four sessions for subsequent removal of new lesions. She has regular follow-up and monitoring for recurrence and metastasis.

DISCUSSION

Trichoepitheliomas present as sporadic, skin-colored papules appearing in childhood or early adolescence.^{1,3,4} When presenting as multiple lesions, genetic syndromes must be considered.

Brooke-Spiegler syndrome is a genodermatosis, which presents with various cutaneous neoplasms including trichoepitheliomas, cylindromas, and spiradenomas commonly on the head and neck.^{1,5} This is caused by mutations in the *CYLD* gene on chromosome 16q12-q13, which codes for CYLD. CYLD inactivation results in uncontrolled cellular proliferation and development of adnexal tumors.⁵

Rare cases of malignant transformation of trichoepitheli-



Figure 4. Clinical photos at **A.** baseline, **B.** 1 week, **C.** 3 weeks, and **D.** 16 weeks post-CO₂ laser ablation and debulking of ulcerated and friable pigmented lesions

omas, especially in long-standing ones, as well as metastasis, have been reported with unknown exact incidence rates.⁴ Clinical signs include pain, bleeding, ulceration, and rapid growth.^{2,5} In Brooke-Spiegler syndrome, malignant transformation of pre-existing benign neoplasms has been reported in 5–10% of patients.¹ Moreover, cases wherein basal cell carcinoma co-existed in adjacent sites and not on pre-existing trichoepitheliomas have been reported. These have been considered “collision tumors” wherein the lesions independently developed in the same location.²

In our patient, some of the skin-colored papules acquired pigmentation and ulceration, features not seen in trichoepithelioma. Biopsies of these lesions revealed basal cell carcinoma. All ulcerated lesions were on the face and none were on sun-protected areas. This suggests that some trichoepitheliomas may have transformed into basal cell carcinomas with chronic sun exposure as the inciting factor.

The study of Zaballos et al. showed that on dermoscopy, trichoepitheliomas exhibit thin, in-focus arborizing vessels, shiny white areas, blue-gray dots, and yellowish-brown background. Basal cell carcinomas show leaf-like areas, blue-gray ovoid nests, brown pigment, branch-like arborizing telangiectasia, and spoke-wheel areas.⁶ These are consistent with the dermoscopic findings of our patient.

Histologically, trichoepitheliomas appear as symmetrical, well-circumscribed, dermal tumors composed of basaloid cells with peripheral palisading, surrounded by fibrous stroma with clefts between collagen bundles. Characteristic features include horn cysts and papillary mesenchymal bodies, but their

absence does not rule out trichoepitheliomas.^{2,4,7} In our patient, some lesions showed features of trichoepithelioma. However, biopsies from ulcerated lesions exhibited islands of atypical basaloid cells throughout the dermis and into the subcutis, artifactual clefts around the basaloid cells, areas of necrosis, and scattered melanophages. These are characteristic findings of basal cell carcinoma and not seen in trichoepithelioma.

Trichoepitheliomas are CD34+/CK20+/CK15+/PHLDA1-/BerEP4-, while basal cell carcinomas are BerEP4+/CD34-/CK20-/CK15-/PHLDA1-. Immunohistochemistry is useful in differentiating between the two entities, but it can distinguish them in only in 36% of cases, thus routine histology with clinical correlation is still the diagnostic gold standard.⁷ Small, skin-colored lesions from our patient were negative for BerEP4, while large hyperpigmented lesions stained positive for BerEP4. This denoted that our patient presented with both trichoepitheliomas and basal cell carcinomas.

Treatment of trichoepitheliomas is not routine because they are asymptomatic and benign. However, treatment may be indicated for cosmetic purposes or malignancy. For solitary lesions, the treatment of choice is surgical excision with narrow margins.^{8,9} For multiple lesions, treatment modalities include cryosurgery, chemical cauterization, dermabrasion, and others. However, they have shown varied results. Potential complica-

tions include increased recurrence, permanent scarring, hypopigmentation, and atrophy. Non-surgical interventions such as 5% imiquimod cream and tretinoin 1% gel have shown favorable results.^{8,9} However, these are not effective for big lesions similar to those in our patient.

In our patient, ablative CO₂ laser was used because of its minimal side effects and satisfactory cosmetic outcomes.¹⁰ Due to the widespread extent of lesions, excision of all lesions was impossible and could lead to further disfigurement. Therefore, our treatment goal was to remove and debulk only the ulcerated and friable pigmented lesions. The patient was satisfied with the outcome and has undergone several sessions to remove new friable lesions.

CONCLUSION

A case of malignant transformation of trichoepitheliomas into basal cell carcinomas in a Filipino-American female with Brooke-Spiegler syndrome was presented. Thorough clinical and histopathological assessments are necessary to diagnose malignant transformation so that appropriate management could be instituted. CO₂ laser ablation may be used to remove ulcerated lesions with satisfactory cosmetic outcomes. Impingement of lesions on other organs may lead to complications, therefore a multi-disciplinary team is warranted.

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